FAMILIAL ISOLATED PITUITARY ADENOMA – OMIM: +102200, 605555

INTRODUCTION
Pituitary tumours account for ~15% of intracranial tumours. Most pituitary adenomas are sporadic but a proportion are associated with familial syndromes (MEN1, Carney complex and MEN1-like) where they are often associated with other clinical features. Mutations in the aryl hydrocarbon receptor-interacting protein (AIP) gene predispose individuals to familial isolated pituitary adenoma (FIPA) without the characteristics of other abnormalities associated with familial pituitary adenoma syndromes. Germline mutations in AIP account for ~15-20% cases FIPA and families with AIP mutations are generally characterised by young onset somatotroph or lactotroph macroadenomas and associated acromegaly. The mean age of diagnosis is 20-24 years of age and inheritance is autosomal dominant. The penetrance of germline mutations is variable (average 15-30%, although a range of 10-80% has been quoted).

AIP mutations have also been identified in patients with no family history and young-onset (<30 years) pituitary adenomas which are mostly growth-hormone secreting, and occasionally prolactin and ACTH secreting. In some cases the lack of family history may be due to incomplete penetrance of the mutation.

TESTING AND REFERRALS
Diagnostic:
- Clinically affected patients (see strategy below). UK diagnostic referrals are accepted from Clinical Genetics, Endocrinology and consultants from other relevant specialties

Carrier/Presymptomatic/Test for Familial Mutation:
- Relatives of clinically affected patients/patients at risk of developing FIPA -familial mutation known.
- Presymptomatic referrals should ideally be referred through/in collaboration with Clinical Genetics departments.

Prenatal:
- Prenatal testing is not generally requested but if required must be discussed with the laboratory and arranged in advance. Referrals are only accepted from Clinical Genetics.

STRATEGY
Molecular analysis of AIP is recommended in patients with a pituitary adenoma (and no other associated features) who have any of the following;
1. A family history of pituitary adenoma
2. Childhood onset of pituitary adenoma
3. A pituitary somatroph or lactotroph macroadenoma diagnosed before the age of 30 years

Once a pathogenic mutation has been identified in an individual, testing for that variant is available to other at-risk or affected family members.

TECHNICAL INFORMATION
- Sanger sequencing analysis of exons 1-6 of the AIP gene, and MLPA analysis for detection of deletions and duplications of one or more exon.
- Analytical sensitivity- this analysis detects approx. 99% of sequence variants within the coding region and exon-intron boundaries of AIP, and also deletions/duplications of one or more exon
- Clinical Sensitivity: Intragenic mutations in AIP account for ~15-20% of cases of FIPA and ~5% of cases of sporadic acromegaly.

TARGET REPORTING TIMES
Diagnostic test: 40 days
Carrier/Presymptomatic/Familial Mutation test: 10 days

N.B. Details are correct for the date of printing only – last updated 14/07/2015